<110> ZAPHIROPOULOS, Peter et al.

<120> A NOVEL COMPONENT IN THE HEDGEHOG SIGNALLING PATHWAY

<130> 2921-0130P

<140> 09/807,007
<141> 2001-04-06

<160> 16

<170> PatentIn version 3.1

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<212> PRT
<213> Homo sapiens

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Pro Leu Trp Leu Arg Ala Tyr Phe Gln Gly Leu Leu Phe Ser Leu Gly
        35                  40                  45


Cys Gly Ile Gln Arg His Cys Gly Lys Val Leu Phe Leu Gly Leu Leu
    50                  55                  60


Ala Phe Gly Ala Leu Ala Leu Gly Leu Arg Met Ala Ile Ile Glu Thr
65                  70                  75                  80


Asn Leu Glu Gln Leu Trp Val Glu Val Gly Ser Arg Val Ser Gln Glu
                85                  90                  95


Leu His Tyr Thr Lys Glu Lys Leu Gly Glu Glu Ala Ala Tyr Thr Ser
            100                 105                 110


Gln Met Leu Ile Gln Thr Ala Arg Gln Glu Gly Glu Asn Ile Leu Thr
            115                 120                 125


Pro Glu Ala Leu Gly Leu His Leu Gln Ala Ala Leu Thr Ala Ser Lys
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Val Gln Val Ser Leu Tyr Gly Lys Ser Trp Asp Leu Asn Lys Ile Cys
145                 150             155                 160

Tyr Lys Ser Gly Val Pro Leu Ile Glu Asn Gly Met Ile Glu Arg Met
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Ile Glu Lys Leu Phe Pro Cys Val Ile Leu Thr Pro Leu Asp Cys Phe
                180             185                 190

Trp Glu Gly Ala Lys Leu Gln Gly Gly Ser Ala Tyr Leu Pro Gly Arg
            195                 200             205

Pro Asp Ile Gln Trp Thr Asn Leu Asp Pro Glu Gln Leu Leu Glu Glu
    210             215             220

Leu Gly Pro Phe Ala Ser Leu Glu Gly Phe Arg Glu Leu Leu Asp Lys
225             230             235             240

Ala Gln Val Gly Gln Ala Tyr Val Gly Arg Pro Cys Leu His Pro Asp
            245             250             255

Asp Leu His Cys Pro Pro Ser Ala Pro Asn His His Ser Arg Gln Ala
        260             265             270

Pro Asn Val Ala His Glu Leu Ser Gly Gly Cys His Gly Phe Ser His
        275             280             285

Lys Phe Met His Trp Gln Glu Glu Leu Leu Leu Gly Gly Met Ala Arg
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Asp Pro Gln Gly Glu Leu Leu Arg Ala Glu Ala Leu Gln Ser Thr Phe
305             310             315             320

Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu His Phe Arg Gly Asp Tyr
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Gln Thr His Asp Ile Gly Trp Ser Glu Glu Gln Ala Ser Thr Val Leu
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Gln Ala Trp Gln Arg Arg Phe Val Gln Leu Ala Gln Glu Ala Leu Pro
    355             360             365
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2

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Glu Asn Ala Ser Gln Gln Ile His Ala Phe Ser Ser Thr Thr Leu Asp
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Asp Ile Leu His Ala Phe Ser Glu Val Ser Ala Ala Arg Val Val Gly
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Gly Tyr Leu Leu Met Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp
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Asp Cys Ala Gln Ser Gln Gly Ser Val Gly Leu Ala Gly Val Leu Leu
                420                 425                 430

Val Ala Leu Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly
            435                 440                 445

Ile Thr Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu
    450                 455                 460

Gly Ile Gly Val Asp Asp Val Phe Leu Leu Ala His Ala Phe Thr Glu
465                 470                 475                 480

Ala Leu Pro Gly Thr Pro Leu Gln Glu Arg Met Gly Glu Cys Leu Gln
                485                 490                 495

Arg Thr Gly Thr Ser Val Val Leu Thr Ser Ile Asn Asn Met Ala Ala
                500                 505                 510

Phe Leu Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg Ala Phe Ser
            515                 520                 525

Leu Gln Ala Ala Ile Val Val Gly Cys Thr Phe Val Ala Val Met Leu
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Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg Arg Arg His Cys Gln
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Arg Leu Asp Val Leu Cys Cys Phe Ser Ser Pro Cys Ser Ala Gln Val
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Ile Gln Ile Leu Pro Gln Glu Leu Gly Asp Gly Thr Val Pro Val Gly
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Ile Ala His Leu Thr Ala Thr Val Gln Ala Phe Thr His Cys Glu Ala
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Pro Pro Pro Ser Asp Pro Leu Gly Ser Glu Leu Phe Ser Pro Gly Gly
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Ser Thr Arg Asp Leu Leu Gly Gln Glu Glu Glu Thr Arg Gln Lys Ala
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Ala Cys Lys Ser Leu Pro Cys Ala Arg Trp Asn Leu Ala His Phe Ala
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Arg Tyr Gln Phe Ala Pro Leu Leu Leu Gln Ser His Ala Lys Ala Ile
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Val Leu Val Leu Phe Gly Ala Leu Leu Gly Leu Ser Leu Tyr Gly Ala
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Thr Leu Val Gln Asp Gly Leu Ala Leu Thr Asp Val Val Pro Arg Gly
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Thr Lys Glu His Ala Phe Leu Ser Ala Gln Leu Arg Tyr Phe Ser Leu
            725   730   735

Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala His Ser
          740   745   750

Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser Leu Lys Ala
      755   760   765

Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr Trp Leu His Tyr
    770   775   780

Tyr Arg Asn Trp Leu Gln Gly Ile Gln Ala Ala Phe Asp Gln Asp Trp
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Ala Ser Gly Arg Ile Thr Arg His Ser Tyr Arg Asn Gly Ser Glu Asp
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4

Gly Ala Leu Ala Tyr Lys Leu Leu Ile Gln Thr Gly Asp Ala Gln Glu
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Leu Leu Asp Phe Ser Gln Leu Thr Thr Arg Lys Leu Val Asp Arg Glu
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Gly Leu Ile Pro Pro Glu Leu Phe Tyr Met Gly Leu Thr Val Trp Val
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Ser Ser Asp Pro Leu Gly Leu Ala Ala Ser Gln Ala Asn Phe Tyr Pro
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Pro Pro Pro Glu Trp Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn
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Phe Arg Ile Pro Pro Ala Gln Pro Leu Glu Phe Ala Gln Phe Pro Phe
                900   905   910

Leu Leu Arg Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu
                915   920   925

Gly Ala Arg Ala Ala Cys Ala Glu Ala Gly Gln Ala Gly Val His Ala
      930   935   940

Tyr Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu
945   950   955   960

Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr Phe
                965   970   975

Leu Val Cys Ala Leu Leu Leu Leu Asn Pro Trp Thr Ala Gly Leu Ile
                980   985   990

Val Leu Val Leu Ala Met Met Thr Val Glu Leu Phe Gly Ile Met Gly
      995   1000   1005

Phe Leu Gly Ile Lys Leu Ser Ala Ile Pro Val Val Ile Leu Val
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Ala Ser Val Gly Ile Gly Val Glu Phe Thr Val His Val Ala Leu
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5

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Gly Phe  Leu Thr Thr Gln Gly  Ser Arg Asn Leu Arg  Ala Ala His
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Thr Leu  Leu Gly Leu Leu Met  Leu Ala Gly Ser His  Phe Asp Phe
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Ile Val  Arg Tyr Phe Phe Ala  Ala Leu Thr Val Leu  Thr Leu Leu
    1085                 1090                 1095

Gly Leu  Leu His Gly Leu Val  Leu Leu Pro Val Leu  Leu Ser Ile
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Leu Gly  Pro Pro Pro Glu Val  Ile Gln Met Tyr Lys  Glu Ser Pro
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6

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7

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11

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13

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14

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16

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<213> Homo sapiens

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            20                  25                  30

Arg Arg Arg Thr Gly Gly Leu Arg Arg Ala Ala Ala Pro Asp Arg Asp
            35                  40                  45

Tyr Leu His Arg Pro Ser Tyr Cys Asp Ala Ala Phe Ala Leu Glu Gln
        50                  55                  60

Ile Ser Lys Gly Lys Ala Thr Gly Arg Lys Ala Pro Leu Trp Leu Arg
65                  70                  75                  80

Ala Lys Phe Gln Arg Leu Leu Phe Lys Leu Gly Cys Tyr Ile Gln Lys
                85                  90                  95

Asn Cys Gly Lys Phe Leu Val Val Gly Leu Leu Ile Phe Gly Ala Phe
            100                 105                 110

Ala Val Gly Leu Lys Ala Ala Asn Leu Glu Thr Asn Val Glu Glu Leu
            115                 120                 125

Trp Val Glu Val Gly Gly Arg Val Ser Arg Glu Leu Asn Tyr Thr Arg
        130                 135                 140

Gln Lys Ile Gly Glu Glu Ala Met Phe Asn Pro Gln Leu Met Ile Gln
145                 150                 155                 160

Thr Pro Lys Glu Glu Gly Ala Asn Val Leu Thr Thr Glu Ala Leu Leu
                165                 170                 175

Gln His Leu Asp Ser Ala Leu Gln Ala Ser Arg Val His Val Tyr Met
            180                 185                 190
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17

Tyr Asn Arg Gln Trp Lys Leu Glu His Leu Cys Tyr Lys Ser Gly Glu
195   200   205

Leu Ile Thr Glu Thr Gly Tyr Met Asp Gln Ile Ile Glu Tyr Leu Tyr
210   215   220

Pro Cys Leu Ile Ile Thr Pro Leu Asp Cys Phe Trp Glu Gly Ala Lys
225   230   235   240

Leu Gln Ser Gly Thr Ala Tyr Leu Leu Gly Lys Pro Pro Leu Arg Trp
245   250   255

Thr Asn Phe Asp Pro Leu Glu Phe Leu Glu Glu Leu Lys Lys Ile Asn
260   265   270

Tyr Gln Val Asp Ser Trp Glu Glu Met Leu Asn Lys Ala Glu Val Gly
275   280   285

His Gly Tyr Met Asp Arg Pro Cys Leu Asn Pro Ala Asp Pro Asp Cys
290   295   300

Pro Ala Thr Ala Pro Asn Lys Asn Ser Thr Lys Pro Leu Asp Met Ala
305   310   315   320

Leu Val Leu Asn Gly Gly Cys His Gly Leu Ser Arg Lys Tyr Met His
325   330   335

Trp Gln Glu Glu Leu Ile Val Gly Gly Thr Val Lys Asn Ser Thr Gly
340   345   350

Lys Leu Val Ser Ala His Ala Leu Gln Thr Met Phe Gln Leu Met Thr
355   360   365

Pro Lys Gln Met Tyr Glu His Phe Lys Gly Tyr Glu Tyr Val Ser His
370   375   380

Ile Asn Trp Asn Glu Asp Lys Ala Ala Ala Ile Leu Glu Ala Trp Gln
385   390   395   400

Arg Thr Tyr Val Glu Val Val His Gln Ser Val Ala Gln Asn Ser Thr
405   410   415

18

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Gln Lys Val Leu Ser Phe Thr Thr Thr Thr Leu Asp Asp Ile Leu Lys
          420             425             430

Ser Phe Ser Asp Val Ser Val Ile Arg Val Ala Ser Gly Tyr Leu Leu
          435             440             445

Met Leu Ala Tyr Ala Cys Leu Thr Met Leu Arg Trp Asp Cys Ser Lys
          450             455             460

Ser Gln Gly Ala Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu Ser
465             470             475             480

Val Ala Ala Gly Leu Gly Leu Cys Ser Leu Ile Gly Ile Ser Phe Asn
              485             490             495

Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly Val Gly Val
          500          .      505             510

Asp Asp Val Phe Leu Leu Ala His Ala Phe Ser Glu Thr Gly Gln Asn
          515             520             525

Lys Arg Ile Pro Phe Glu Asp Arg Thr Gly Glu Cys Leu Lys Arg Thr
          530             535             540

Gly Ala Ser Val Ala Leu Thr Ser Ile Ser Asn Val Thr Ala Phe Phe
545             550             555             560

Met Ala Ala Leu Ile Pro Ile Pro Ala Leu Arg Ala Phe Ser Leu Gln
              565             570             575

Ala Ala Val Val Val Val Phe Asn Phe Ala Met Val Leu Leu Ile Phe
          580             585             590

Pro Ala Ile Leu Ser Met Asp Leu Tyr Arg Arg Glu Asp Arg Arg Leu
          595             600             605

Asp Ile Phe Cys Cys Phe Thr Ser Pro Cys Val Ser Arg Val Ile Gln
          610             615             620

Val Glu Pro Gln Ala Tyr Thr Asp Thr His Asp Asn Thr Arg Tyr Ser
625             630             635             640
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19

Pro Pro Pro Pro Tyr Ser Ser His Ser Phe Ala His Glu Thr Gln Ile
            645   650   655

Thr Met Gln Ser Thr Val Gln Leu Arg Thr Glu Tyr Asp Pro His Thr
            660   665   670

His Val Tyr Tyr Thr Thr Ala Glu Pro Arg Ser Glu Ile Ser Val Gln
            675   680   685

Pro Val Thr Val Thr Gln Asp Thr Leu Ser Cys Gln Ser Pro Glu Ser
    690   695   700

Thr Ser Ser Thr Arg Asp Leu Leu Ser Gln Phe Ser Asp Ser Ser Leu
705   710   715   720

His Cys Leu Glu Pro Pro Cys Thr Lys Trp Thr Leu Ser Ser Phe Ala
                725   730   735

Glu Lys His Tyr Ala Pro Phe Leu Leu Lys Pro Lys Ala Lys Val Val
                740   745   750

Val Ile Phe Leu Phe Leu Gly Leu Leu Gly Val Ser Leu Tyr Gly Thr
            755   760   765

Thr Arg Val Arg Asp Gly Leu Asp Leu Thr Asp Ile Val Pro Arg Glu
    770   775   780

Thr Arg Glu Tyr Asp Phe Ile Ala Ala Gln Phe Lys Tyr Phe Ser Phe
785   790   795   800

Tyr Asn Met Tyr Ile Val Thr Gln Lys Ala Asp Tyr Pro Asn Ile Gln
                805   810   815

His Leu Leu Tyr Asp Leu His Arg Ser Phe Ser Asn Val Lys Tyr Val
                820   825   830

Met Leu Glu Glu Asn Lys Gln Leu Pro Lys Met Trp Leu His Tyr Phe
            835   840   845

Arg Asp Trp Leu Gln Gly Leu Gln Asp Ala Phe Asp Ser Asp Trp Glu
    850   855   860

20

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Thr Gly Lys Ile Met Pro Asn Asn Tyr Lys Asn Gly Ser Asp Asp Gly
865                 870             875             880

Val Leu Ala Tyr Lys Leu Leu Val Gln Thr Gly Ser Arg Asp Lys Pro
                885             890             895

Ile Asp Ile Ser Gln Leu Thr Lys Gln Arg Leu Val Asp Ala Asp Gly
            900             905             910

Ile Ile Asn Pro Ser Ala Phe Tyr Ile Tyr Leu Thr Ala Trp Val Ser
            915             920             925

Asn Asp Pro Val Ala Tyr Ala Ala Ser Gln Ala Asn Ile Arg Pro His
    930             935             940

Arg Pro Glu Trp Val His Asp Lys Ala Asp Tyr Met Pro Glu Thr Arg
945             950             955             960

Leu Arg Ile Pro Ala Ala Glu Pro Ile Glu Tyr Ala Gln Phe Pro Phe
            965             970             975

Tyr Leu Asn Gly Leu Arg Asp Thr Ser Asp Phe Val Glu Ala Ile Glu
            980             985             990

Lys Val Arg Thr Ile Cys Ser Asn  Tyr Thr Ser Leu Gly  Leu Ser Ser
            995             1000            1005

Tyr Pro  Asn Gly Tyr Pro Phe  Leu Phe Trp Glu Gln  Tyr Ile Gly
    1010            1015            1020

Leu Arg  His Trp Leu Leu Leu  Phe Ile Ser Val Val  Leu Ala Cys
    1025            1030            1035

Thr Phe  Leu Val Cys Ala Val  Phe Leu Leu Asn Pro  Trp Thr Ala
    1040            1045            1050

Gly Ile  Ile Val Met Val Leu  Ala Leu Met Thr Val  Glu Leu Phe
    1055            1060            1065

Gly Met  Met Gly Leu Ile Gly  Ile Lys Leu Ser Ala  Val Pro Val
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21

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Val Ile  Leu Ile Ala Ser Val  Gly Ile Gly Val Glu  Phe Thr Val
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His Val  Ala Leu Ala Phe Leu  Thr Ala Ile Gly Asp  Lys Asn Arg
    1100                1105                1110

Arg Ala  Val Leu Ala Leu Glu  His Met Phe Ala Pro  Val Leu Asp
    1115                1120                1125

Gly Ala  Val Ser Thr Leu Leu  Gly Val Leu Met Leu  Ala Gly Ser
    1130                1135                1140

Glu Phe  Asp Phe Ile Val Arg  Tyr Phe Phe Ala Val  Leu Ala Ile
    1145                1150                1155

Leu Thr  Ile Leu Gly Val Leu  Asn Gly Leu Val Leu  Leu Pro Val
    1160                1165                1170

Leu Leu  Ser Phe Phe Gly Pro  Tyr Pro Glu Val Ser  Pro Ala Asn
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Gly Leu  Asn Arg Leu Pro Thr  Pro Ser Pro Glu Pro  Pro Pro Ser
    1190                1195                1200

Val Val  Arg Phe Ala Met Pro  Pro Gly His Thr His  Ser Gly Ser
    1205                1210                1215

Asp Ser  Ser Asp Ser Glu Tyr  Ser Ser Gln Thr Thr  Val Ser Gly
    1220                1225                1230

Leu Ser  Glu Glu Leu Arg His  Tyr Glu Ala Gln Gln  Gly Ala Gly
    1235                1240                1245

Gly Pro  Ala His Gln Val Ile  Val Glu Ala Thr Glu  Asn Pro Val
    1250                1255                1260

Phe Ala  His Ser Thr Val Val  His Pro Glu Ser Arg  His His Pro
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Pro Ser  Asn Pro Arg Gln Gln  Pro His Leu Asp Ser  Gly Ser Leu
    1280                1285                1290
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22

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Pro Pro  Gly Arg Gln Gly Gln  Gln Pro Arg Arg Asp  Pro Pro Arg
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Glu Gly  Leu Trp Pro Pro Leu  Tyr Arg Pro Arg Arg  Asp Ala Phe
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Glu Ile  Ser Thr Glu Gly His  Ser Gly Pro Ser Asn  Arg Ala Arg
    1325                 1330                 1335

Trp Gly  Pro Arg Gly Ala Arg  Ser His Asn Pro Arg  Asn Pro Ala
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Ser Thr  Ala Met Gly Ser Ser  Val Pro Gly Tyr Cys  Gln Pro Ile
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Thr Thr  Val Thr Ala Ser Ala  Ser Val Thr Val Ala  Val His Pro
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Pro Pro  Val Pro Gly Pro Gly  Arg Asn Pro Arg Gly  Gly Leu Cys
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Pro Gly  Tyr Pro Glu Thr Asp  His Gly Leu Phe Glu  Asp Pro His
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Val Pro  Phe His Val Arg Cys  Glu Arg Arg Asp Ser  Lys Val Glu
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Val Ile  Glu Leu Gln Asp Val  Glu Cys Glu Glu Arg  Pro Arg Gly
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Ser Ser  Ser Asn
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Val Thr
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<213> Homo sapiens

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Val Thr
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<400> 9

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acc tcc atg acc gtg gcc atc cac cca ccc ccc ctg cct ggt gcc tac    48
Thr Ser Met Thr Val Ala Ile His Pro Pro Pro Leu Pro Gly Ala Tyr
1               5                   10                  15

atc cat                                                            54
Ile His
```

<210> 10
<211> 18
<212> PRT
<213> Homo sapiens

<400> 10

```
Thr Ser Met Thr Val Ala Ile His Pro Pro Pro Leu Pro Gly Ala Tyr
1               5                   10                  15
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24

Ile His

<210> 11
<211> 54
<212> DNA
<213> Homo sapiens

<220>
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<400> 11
cca gcc cct gat gag ccc cct tgg tcc cct gct gcc act agc tct ggc   48
Pro Ala Pro Asp Glu Pro Pro Trp Ser Pro Ala Ala Thr Ser Ser Gly
1   5   10   15

aac ctc   54
Asn Leu

<210> 12
<211> 18
<212> PRT
<213> Homo sapiens

<400> 12

Pro Ala Pro Asp Glu Pro Pro Trp Ser Pro Ala Ala Thr Ser Ser Gly
1   5   10   15

Asn Leu

<210> 13
<211> 33
<212> DNA
<213> Homo sapiens

<220>
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<222> (1)..(33)
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<400> 13
agt tcc agg gga cca ggt cca gcc act ggg tga   33
Ser Ser Arg Gly Pro Gly Pro Ala Thr Gly
1   5   10

25

<210> 14
<211> 10
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<400> 14

Ser Ser Arg Gly Pro Gly Pro Ala Thr Gly
1   5   10

<210> 15
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<220>
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<400> 15
agg ccc gag gag atc tag
Arg Pro Glu Glu Ile
1   5   18

<210> 16
<211> 5
<212> PRT
<213> Homo sapiens

<400> 16

Arg Pro Glu Glu Ile
1   5

B5 CONT.